

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A method for the preparation of human, humanized or chimæric antibodies or polypeptides having different binding profiles, comprising an Fc region of human IgG, ~~said antibodies or polypeptides having different binding profiles~~, wherein said method comprises ~~the steps consisting of~~:
 - a. providing candidate human, humanized or chimæric antibodies or polypeptides comprising the Fc region of human IgG produced naturally by or following transfection with a vector comprising the coding sequence for said antibody or polypeptide ~~into of cells from~~ animal cell lines comprising ~~hybridoma~~ .
hybridomas, heterohybridoma heterohybridomas, EBV-transformed human B cell lines or from eukaryotic microorganisms,
 - b. testing the binding of said antibodies or polypeptides on Fcγ receptors ~~including~~ FcγRIIIA, FcγRIIA and FcγRIIB, and
 - c. selecting antibodies or polypeptides which:
 - i. bind to ~~both~~ FcγRIIIA, FcγRIIA and FcγRIIB, or
 - ii. bind to ~~both~~ FcγRIIA and FcγRIIB but do not bind or bind only weakly to FcγRIIIA, or
 - iii. do not bind or bind only weakly to ~~both~~ FcγRIIIA, FcγRIIA and FcγRIIB.
2. (Currently amended) ~~A~~ The method according to claim 1 wherein said antibodies or polypeptides selected ~~in the step~~:

- c.i) are produced by cells from a lymphoid cell line ~~lines or line~~, a lymphoid-derived cell line ~~lines or hybridomas~~ line, a hybridoma cell line, or from an epithelial kidney cell line, line, ~~said antibodies or polypeptides selected in the step~~
- c. [D]] ii) are produced by cells from a non-lymphoid cell line ~~lines and said antibodies or polypeptides selected in the step~~
- c. [D]] iii) are produced by cells from ~~an a heterohybridoma cell line wherein the non-myeloma fusion partner is fused to cells from an~~ a EBV-transformed cell ~~line or to or a B lymphocytes lymphocyte~~ from human donors.
3. (Currently amended) ~~A~~ The method according to claim 2, wherein
- i. said lymphoid-derived cell ~~lines are~~ line is ~~a rat myeloma cell lines or line~~, the hybridoma YB2/0 cell line (ATCC number CRL-1662) or a cell ~~lines~~ line derived thereof, ~~and/or~~
 - ii. ~~the~~ said epithelial kidney cell line is VERO (ATCC number CCL-81) or a cell ~~lines~~ line derived thereof, ~~and/or~~
 - iii. ~~the~~ said non-lymphoid cell line is CHO (ATCC number CCL-61) or a cell ~~lines~~ line derived thereof ~~and/or~~
 - iv. said heterohybridoma cell line is K6H6B5 (ATCC number CRL-1823) or a cell ~~lines~~ line derived thereof.

4-47 (Canceled)

48. (New) The method according to claim 1, wherein said binding is performed using:
- i. indicator cells from a cell line that express different Fc receptors on their cell surface, or
 - ii. recombinant Fc receptors comprising FcγR ectodomains, Fc receptors derived-peptides.

49. (New) The method according to claim 1, wherein said antibodies or polypeptides selected for their ability to bind to FcgammaRIIIA, FcgammaRIIA and FcgammaRIIB, and said antibodies or polypeptides selected for their ability to bind to FcgammaRIIA and FcgammaRIIB are further selected by a functional assays for their ability

- i. to trigger FcgammaRIIIA leading to improved ADCC, increased production of cytokines such as Interleukin-2 (IL-2) and of pro-inflammatory molecules such as Tumor Necrosis Factor alpha (TNF alpha) and
- ii. to trigger FcgammaRIIB leading to the inhibition of calcium mobilization and to the inhibition of cytokine production such as IL-2 by cells expressing FcgammaRIIB such as B cells and monocytes.

50. (New) The method of claim 49, wherein said functional assays consist of a calcium mobilization inhibition assay, and/or a cytokine secretion inhibition assay.

51. (New) The method of claim 49, wherein said functional assay further comprises a specific FcgammaRIIIA ADCC assay.

52. (New) A method of producing antibodies in a lymphoid cell line, a lymphoid-derived cell line, a hybridoma cell line or an epithelial kidney cell line wherein said antibodies are able to bind to FcgammaRIIIA, FcgammaRIIA and FcgammaRIIB.

53. (New) The method of claim 52, wherein said antibodies are immunomodulatory antibodies.

54. (New) The method of claim 52, wherein said antibodies are both immunomodulatory and cytotoxic antibodies.

55. (New) The method of claim 52, wherein said hybridoma cell line is YB2/0.

56. (New) The method of claim 52, wherein said epithelial kidney cell line is VERO (ATCC number CCL-81).

57. (New) A method of producing antibodies in a non-lymphoid cell line wherein said antibodies bind FcγRIIA and FcγRIIB but do not bind or bind only weakly to FcγRIIA.

58. (New) The method of claim 57, wherein said antibodies are immunomodulatory antibodies.

59. (New) The method of claim 57, wherein said antibodies induce ADCC and phagocytosis by monocytes and macrophages expressing FcγRIIA.

60. (New) The method of claim 57, wherein said cells from a non-lymphoid cell line is CHO (ATCC number CCL-61).

61. (New) A method of producing antibodies in heterohybridoma fused to cells from an EBV-transformed cell line, or B cells, wherein said antibodies do not bind or bind weakly to FcγRIIA, FcγRIIA and FcγRIIB.

62. (New) The method of claim 61, wherein said antibodies are used as a therapeutic alternative to the use of IgG4.

63. (New) The method of claim 61, wherein said heterohybridoma is K6H6B5 (ATCC number CRL-1823) fused to human B cells.

64. (New) A composition comprising an antibody or polypeptide identified by the method of claim 1, wherein said antibody or polypeptide contains 10% to 55% fucose, and 60% to 98% galactose.

65. (New) The composition of claim 64, wherein said antibody or polypeptide is produced by cells from a lymphoid cell line, a lymphoid-derived cell line, a hybridoma cell line or an epithelial kidney cell line.

66. (New) The composition of claim 65, wherein said hybridoma cell line is the YB2/0 cell line (ATCC number CRL-1662).

67. (New) The composition of claim 65, wherein said epithelial kidney cell line is VERO (ATCC number CCL-81).

68. (New) The composition of claim 64, wherein said antibody or polypeptide binds to FcgammaRIIA, FcgammaRIIA and FcgammaRIIB.

69. (New) A composition comprising an antibody or a polypeptide identified by the method of claim 1, wherein said antibody or polypeptide contains 70% to 100% fucose, and 60% to 98% galactose.

70. (New) The composition of claim 69, wherein said antibody or polypeptide is produced by cells from a non-lymphoid cell line.

71. (New) The composition of claim 70, wherein said non-lymphoid cell line is the CHO cell line (ATCC number CCL-61).

72. (New) The composition of claim 69, wherein said antibody or polypeptide binds to FcgammaRIIA and FcgammaRIIB but does not bind or binds only weakly to FcgammaRIIA.

73. (New) A composition comprising an antibody or a polypeptide obtained by the method of claim 1, wherein said antibody or polypeptide contains 80% to 100% fucose, 60% to 98% galactose and 30% to 80% sialylated forms.

74. (New) The composition of claim 73, wherein said antibody or polypeptide is produced by cells from a heterohybridoma fused to EBV-transformed cells or to B lymphocytes from human donors.

75. (New) The antibody or a polypeptide according to claim 74, wherein said heterohybridoma is K6H6B5 (ATCC number CRL-1823) fused to cells from an EBV-transformed cell line.

76. (New) The antibody or polypeptide of claim 73, wherein said antibody or polypeptide does not bind or binds only weakly to both FcgammaRIIA, FcgammaRIIA and FcgammaRIIB.

77. (New) An antibody or a polypeptide identified by steps c.i) to c.iii) of claim 1.
78. (New) The composition of claim 64, wherein said antibody or a polypeptide is an IgG1.
79. (New) The composition of claim 64, wherein said antibody or a polypeptide is an IgG3.
80. (New) The composition of claim 64, wherein said composition comprises at least 80%, of said antibodies or polypeptides.
81. (New) A method of treating cancer, auto-immune diseases, allergies, allo-immunization following transplantation, materno-fetal allo-immunization, Graft-Versus Host (GVH) reaction or infectious diseases comprising administering to a subject in need thereof the composition of claim 80.
82. (New) The method of claim 81, wherein said cancer is leukemia, lymphoma, myeloma, Sezary syndrome, or solid tumors.
83. (New) The method of claim 81, wherein said materno-fœtal allo-immunization is the hemolytic disease of the newborn (HDNB).
84. (New) The method of claim 81, wherein said auto-immune disease is an autoimmune disease involving B cells that produce auto-antibodies such as Systemic Lupus Erythematosus (SLE), Idiopathic Thrombocytopenic Purpura (ITP), Kawasaki syndrome.
85. (New) The method of claim 81, wherein said allergies are asthma, allergic rhinitis, allergic sinusitis, anaphylactic syndrome, urticaria, angioedema, atopic dermatitis, allergic contact dermatitis and erythema.
86. (New) A composition of claim 69 comprising at least 80% antibodies or polypeptides.
87. (New) A method of treating auto-immune diseases, materno-fœtal allo-immunization, and inflammatory diseases comprising administering to a subject in need thereof, the composition of claim 86.
88. (New) A composition of claim 73 comprising at least 80% antibodies or polypeptides.

89. (New) A method of treating inflammatory disease, Crohn's disease or Rheumatoid Arthritis comprising administering to a subject in need thereof the composition of claim 88.
90. (New) The composition of claim 69, wherein said antibody or polypeptide is IgG1.
91. (New) The composition of claim 73, wherein said antibody or polypeptide is an IgG1.
92. (New) The composition of claim 69, wherein said antibody or a polypeptide is an IgG3.
93. (New) The composition of claim 73, wherein said antibody or a polypeptide is an IgG3.
94. (New) The method of claim 50, wherein said functional assay further comprises a specific FcgammaRIIIA ADCC assay.
95. (New) The method of claim 50, wherein said functional assay further comprises a specific FcgammaRIIIA ADCC assay.
96. (New) The method of claim 53, wherein said antibodies are both immunomodulatory and cytotoxic antibodies.
97. (New) The method of claim 58, wherein said antibodies induce ADCC and phagocytosis by monocytes and macrophages expressing FcgammaRIIA.
98. (New) The method of claim 62, wherein said heterohybridoma is K6H6B5 (ATCC number CRL-1823) fused to human B cells.